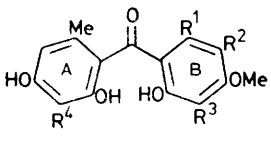
Base Catalysed and Thermal Rearrangements of Grisadiendiones to Depsidones

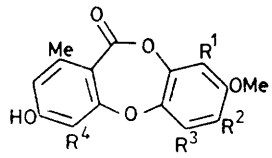
By TONY SALA and MELVYN V. SARGENT*
(*Department of Organic Chemistry, University of Western Australia, Nedlands W.A. 6009, Australia*)

Summary Appropriately substituted grisadiendiones, synthesized by oxidative coupling of benzophenones, undergo base catalysed and thermal rearrangements to depsidones; the mechanisms and the biosynthetic significance of these reactions are discussed.

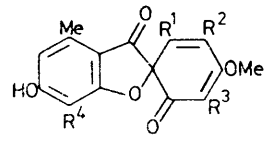
WE have previously shown[1,2] that treatment of the benzophenones (**1**) and (**2**) with potassium hexacyanoferrate(III) in aqueous potassium carbonate solution gave the depsidones (**4**) and (**5**) in excellent yields. We reasoned[3] that the initially formed species in these oxidations were the phenoxy radicals at the positions *ortho* to the carbonyl groups on the A-rings of the benzophenones rather than on the halogenated B-rings which would be expected to be of higher potential. Homolytic aromatic substitution followed by loss of an electron would then yield the grisadiendiones (**7**) and (**8**), presumed to be the intermediates, but not isolated. The mechanism of the conversion of the grisadiendiones (**7**) and (**8**) to the depsidones (**4**) and (**5**) was open to speculation.[1,2] We now present results which throw light on this easy conversion.



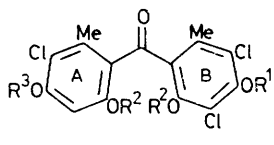
(1) $R^1 = R^3 = R^4 = Me$, $R^2 = Cl$
(2) $R^1 = CH(Me)CH_2Me$, $R^2 = Br$, $R^3 = Me$, $R^4 = H$
(3) $R^1 = R^3 = Me$, $R^2 = Cl$, $R^4 = H$



(4) $R^1 = R^3 = R^4 = Me$, $R^2 = Cl$
(5) $R^1 = Me$, $R^2 = Br$, $R^3 = CH(Me)CH_2Me$, $R^4 = H$
(6) $R^1 = R^3 = Me$, $R^2 = Cl$, $R^4 = H$

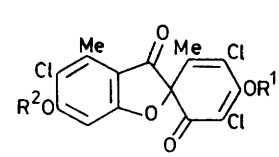


(7) $R^1 = R^3 = R^4 = Me$, $R^2 = Cl$
(8) $R^1 = CH(Me)CH_2Me$, $R^2 = Br$, $R^3 = Me$, $R^4 = H$
(9) $R^1 = R^3 = Me$, $R^2 = Cl$, $R^4 = H$

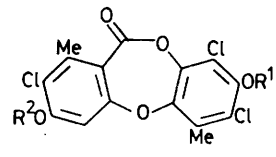


(10) $R^1 = Me$, $R^2 = R^3 = H$
(11) $R^1 = R^2 = R^3 = H$
(12) $R^1 = R^3 = Me$, $R^2 = H$

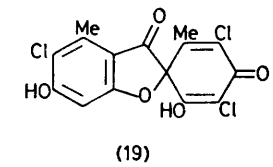
Brief (30–120 s) oxidation of the benzophenones (**1**),[1] (**2**),[2] and (**3**)[3] under the above conditions gave excellent yields of the grisadiendiones (**7**)—(**9**)† the structures of which followed from their elementary analyses and spectroscopic properties. When these oxidations were conducted for an extended period (*ca.* 3 h) the depsidones (**4**)—(**6**) were isolated in excellent yields; hence the grisadiendiones are intermediates. Similarly, brief oxidation (30 s) of the benzophenone (**10**) gave the grisadiendione (**13**). When the oxidation of the benzophenone (**10**) was allowed to continue for 15 min the products were the depsidone (**16**) (45%),



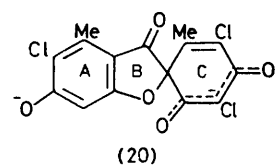
(13) $R^1 = Me$, $R^2 = H$
(14) $R^1 = R^2 = H$
(15) $R^1 = R^2 = Me$



(16) $R^1 = Me$, $R^2 = H$
(17) $R^1 = R^2 = Me$
(18) $R^1 = R^2 = H$



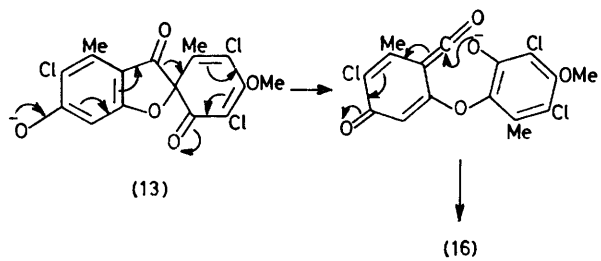
(19)



(20)

identical with the naturally occurring dechlorodiploicin,[4] and a grisadiendione (55%) formulated as the cross conjugated tautomer (**19**), although the spectroscopic data do not exclude the linearly conjugated tautomer (**14**). This grisadiendione (**19**) was also obtained in excellent yield by oxidation of the benzophenone (**11**).

The benzophenone (**12**), however, even on prolonged exposure to the usual oxidizing conditions gave only the grisadiendione (**15**). We therefore postulate that ketens are intermediates in the base catalysed grisadiendione–depsidone rearrangement *e.g.* (**13**) → (**16**) (Scheme 1).



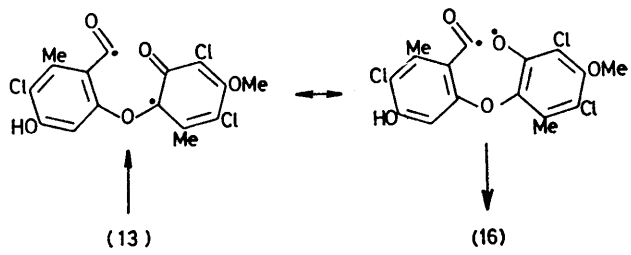
SCHEME 1

The cross conjugated dienone (**19**) thus arises by hydrolysis of the relatively unhindered vinylogous ester function in (**13**). Precedent for the mechanism of this rearrangement is found in the hydrolysis of aryl acetoacetates[5] which occur by an *E*1c*B* mechanism involving a keten only when the leaving group is sufficiently powerful. The grisadiendione (**19**) is therefore unable to rearrange to a depsidone because the ring c phenolate anion (**20**) is a poor leaving group; furthermore, the grisadiendione (**15**) is unable to rearrange under basic conditions because keten formation is blocked.

The grisadiendiones (**7**)—(**9**), (**13**), (**15**), and (**19**) on heating all undergo rearrangement to the related depsidones (**4**)—

† All new compounds gave satisfactory elementary analyses or high resolution mass spectral molecular ion peaks.

(**6**) and (**16**)—(**18**) in high yield. A [1,3] or [1,7] antarafacial sigmatropic shift is allowed by the rules of conservation of orbital symmetry but is probably precluded by unfavourable steric interactions; hence a radical mechanism, *e.g.* (**13**) → (**16**) (Scheme 2) is preferred.



SCHEME 2

The facility of these benzophenone–grisadiendione–depsidone interconversions raises the question of their occurrence in the biosynthesis of depsidones. The currently accepted hypothesis[6] is that depsidones arise by oxidative coupling of *p*-depsides with the direct formation of the seven-membered lactonic ring. Although *p*-depside–depsidone pairs of exactly corresponding structures are known their occurrence is usually confined to widely separated lichen genera.[7] We suggest, in view of the above results, the hypothesis that benzophenones are intermediates on the biosynthetic pathway to depsidones merits serious consideration.

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